Remarks

Upon entry of the foregoing amendment, claims 112-133 are pending in this application. Claims 1-35, 50-77 and 79-111 are canceled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of the cancelled claims either in newly added claims 112-133, above, or in a continuing or divisional application. Claims 112-133 are newly added and are currently under examination. Claims 112 and 132 are the independent claims.

Support for new claim 112 is found, for example, in original claim 1; on page 20, lines 25-26 (for the phrase "not encapsulated by liposomes"); and, elsewhere throughout the specification. Support for the concept of "hydrated skin" is found in examples 1-10; on page 27, lines 9-19; and, elsewhere throughout the specification.

Support for new claim 113 is found, for example, in original claim 2; and, elsewhere throughout the specification.

Support for new claim 114 is found, for example, in original claim 3; and, elsewhere throughout the specification.

Support for new claim 115 is found, for example, in original claim 12; on page 5, lines 34-36; on page 14, lines 20-22; and, elsewhere throughout the specification.

Support for new claim 116 is found, for example, in original claim 14; on page 5, line 37 through page 6, line 2; and, elsewhere throughout the specification.

Support for new claim 117 is found, for example, in original claim 15; and, elsewhere throughout the specification.

Support for new claim 118 is found, for example, on page 14, line 23; and, elsewhere throughout the specification.

Support for new claim 119 is found, for example, on page 14, line 38; and, elsewhere throughout the specification.

Support for new claim 120 is found, for example, on page 15, lines 21-34; on page 18, lines 26-35; and, elsewhere throughout the specification.

Support for new claim 121 is found, for example, on page 17, lines 23-34; and, elsewhere throughout the specification.

Support for new claim 122 is found, for example, on page 16, lines 3-22; and, elsewhere throughout the specification.

Support for new claim 123 is found, for example, on page 16, line 34 through page 17, line 3; and, elsewhere throughout the specification.

Support for new claim 124 is found, for example, on page 17, lines 23-34; and, elsewhere throughout the specification.

Support for new claim 125 is found, for example, on page 18, lines 12-13; and, on page 17, lines 30-31. Support for the phrases "an ADP-ribosylating exotoxin chemically conjugated to a carbohydrate, polypeptide, glycolipid, or glycoprotein; an ADP-ribosylating exotoxin subunit chemically conjugated to a carbohydrate, polypeptide, glycolipid, or glycoprotein; and, an ADP-ribosylating toxoid chemically conjugated to a carbohydrate, polypeptide, glycolipid, or glycoprotein" is found on page 18, lines 1-6; and, elsewhere throughout the specification.

Support for new claim 126 is found, for example, on page 8, lines 19-21; and, elsewhere throughout the specification.

Support for new claim 127 is found, for example, on page 7, lines 9-13; and, elsewhere throughout the specification.

Support for new claim 128 is found, for example, in original claim 6; and, elsewhere throughout the specification.

Support for new claim 129 is found, for example, on page 23, line 5; and, elsewhere throughout the specification.

Support for new claim 130 is found, for example, on page 23, lines 3-16; and, elsewhere throughout the specification.

Support for new claim 131 is found, for example, on page 23, line 10; on page 5, line 4; and, elsewhere throughout the specification.

Support for new claim 132 is found, for example, on page 8, lines 19-21; page 23, lines 9-10; original claim 33; for the concept of "wherein application of the formulation hydrates the skin" on page 5, lines 25-33; and, elsewhere throughout the specification.

Support for new claim 133 is found, for example, on page 23, line 5, lines 8-10; and, elsewhere throughout the specification.

No new matter is believed to have been added by this amendment. In view of the amendments and following remarks, reconsideration of the rejections and withdrawal thereof is respectfully requested.

The Office Action dated June 2, 2003 has been carefully reviewed and the foregoing amendments are made in response thereto.

Comments

New claim 112 had been added and now tracks, in part, the language of original claim 1 and US patent no. 5,910,306 ['306]. A terminal disclaimer over the '306 patent has previously been filed and accepted by the Office.

In order to expedite prosecution of new claims 112 and 132 (and claims 113-131, 133), an explanation of why new claims 112 and 132 (and claims 113-131, 133) continue to be free of the prior art follows.

As is well known by the Examiner, in order to establish a *prima facie* case of obviousness, all claim limitations must be taught or suggested by the prior art. All of the previously cited prior art documents fail to teach or suggest a method of inducing an immune response by applying a formulation comprising, among other elements, an effective amount of antigen which is <u>not</u> encapsulated by liposomes. The instant specification discloses that liposomes are not required to elicit an antigen specific immune response. The addition of liposomes to the formulation (as in, for example, new claim 114) does not change the fact that an effective amount of the antigen which is not encapsulated by liposomes will elicit an antigen specific immune response. Thus, claim 112, and claims 113-131 dependent therefrom, continue to be patentable over USPN 5,340,588 (Domb et al.) and Paul et al. (Document YR, Eur. J. Immunol. 25: 3521 (1995)) for reasons stated by the Office in the June 2003 Office Action. Since claim 112 is believed to be in compliance with paragraph 4 of the Examiner's remarks in the June 2, 2003, Office Action, allowance of independent claim 112 and claims 113-131 dependent therefrom is respectfully requested. New claims 132 and 133 are believed to be free of the art, and allowable, for the same reasons set forth for claims 112-131.

Rejection of claims 1-35, 50-77 and 79-111 under 35 U.S.C. § 112, first paragraph

The Office rejected claims 1-35, 50-77 and 79-11 under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. Claims 1-35, 50-77 and 79-11 have been canceled. Applicants respectfully traverse the rejection and do not believe the rejection applies to new claims 112-131.

The Office asserts the specification and claims as originally filed do not provide support for the invention as now claimed. Specifically mentioned by the Office is the phrase "derivative thereof."

Without acquiescing to the position of the Office, claims 1-35, 50-77 and 79-11 have been canceled and new claims 112-131 added. New claims 112-131 do not contain the phrase "derivative thereof." New claim 122 now recites "toxoids." This amendment is believed to overcome the rejection in view of the statements by the Office (at Office Action page 3, second paragraph) that "The bulk of the disclosure at page 16-18 related to developing toxoids from toxins. Said toxoid might be considered to be adequately described, however, said written description is not adequate for the much broader "derivatives" recited in the claims."

Thus, in view of the new claim language, it is believed the rejection is moot and can be withdrawn. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of claims 1-35, 50-77 and 79-11 under 35 U.S.C. § 112, first paragraph

The Office rejected claims 1-35, 50-77 and 79-111 under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventors had

possession of the claimed invention at the time the application was filed. Applicants respectfully traverse the rejection.

The Office asserts the specification and the claims as originally filed do not provide support for the invention as now claimed for the phrases occuring in quotes :

a. an antigen "which is not encapsulated" (claims 1, 31, 32, 33);

b. wherein a "physical, chemical" electrical or sonic penetration enhancer is not used (claim 4);

c. toxin or "derivative thereof" (claims 25, 26, 85-90 and 108-111);

d. "genetically produced derivative of ADP-ribosylating exotoxin in which ADP-ribosyl transferase activity is inactivated" (claim 51);

e. "chemically produced derivative of ADP-ribosylating exotoxin in which ADP-ribosyl transferase activity is inactivated" (claim 52);

f. "at least partially purified" (claims 54-60 and 96-102); and,

g. "binds a receptor on an antigen presenting cell" (claims 82 and 93).

Applicants acknowledge with appreciation the withdrawal of the rejection of claim 15. Without acquiescing to the position of the Office, Applicants have cancelled claims 1-35, 50-77 and 79-111 and added new claims 112-133. New claims 112-133 do not recite the phrases allegedly lacking support.

The Office (page 4, paragraph 3) remarks that "the disclosure regarding non-encapsulation by liposomes cannot support claims drawn to the more generic non-encapsulation in the absence of liposomes." In reply thereto, claim 112 has been written to change the phrase "not encapsulated," as occurred in the previous claim, to the phrase "not encapsulated by liposomes." The new claim language is believed to overcome the rejection.

Regarding the phrases (d) "genetically produced derivative of ADP-ribosylating exotoxin in which ADP-ribosyl transferase activity is inactivated" (claim 51), and (e) "chemically produced derivative of ADP-ribosylating exotoxin in which ADP-ribosyl transferase activity is inactivated" (claim 52), new claim 125 does not include the wording "genetically produced derivative" or "chemically produced derivative." The new claim language is believed to overcome the rejection.

In view of the cancellation of claims 1-35, 50-77 and 79-111 and the addition of new claims 112-131, the rejections under 35 USC § 112, first paragraph, are believed to be moot. Reconsideration and withdrawal of the rejections is respectfully requested.

Rejection of claims 1-29 (1-35), 50-77 and 79-111 under 35 USC § 112, first paragraph

The Office rejected claims 1-29 (1-35), 50-77 and 79-111 under 35 USC § 112, first paragraph, because the specification does not provide enablement for the phrase "activating a Langerhans cell and "presenting at least one antigen or epitope thereof on a cell surface of the Langerhans cell to a lymphocyte" as set forth in claims 1, 32 and 33. Claims 1-29 (1-35), 50-77 and 79-111 have been canceled and new claims 112-131 added. Applicants respectfully traverse the rejection.

Without acquiescing to the position of the Office, Applicants have canceled the claims containing the above phrases. In view of the cancellation of claims 1-29 (1-35), 50-77 and 79-111 and the addition of new claims 112-133 which do not recite the allegedly non-enabled phrase, the rejection is believed to be moot. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of claims 30, 62-77, 104 and 107 under 35 USC § 112, first paragraph

The Office rejected claims 30, 62-77, 104 and 107 under 35 USC § 112, first paragraph, because the specification is not enabling for a method of inducing an immune response comprising applying an adjuvant only. Applicants respectfully traverse the rejection.

Claims 30, 62-77, 104 and 107 have been canceled and new claims 112-133 added. No new claim is directed to the method of inducing an immune response comprising applying an adjuvant only. Applicants are pursuing claims directed to the subject matter of the cancelled claims in related U.S. patent application no. 09/337,746. However, although the cancellation of the claims moots the rejection, Applicants strenuously disagree with the position of the Office on this issue.

The attention of the Office is directed to specification page 32, Example 1, demonstrating an immune response using CT alone in Table 1 and in Table 5 (page 36); to page 34, showing an immune response to LT alone in Table 3 and in Table 4 (page 35); to page 37, showing an immune response to ETA alone in Table 6; and, to page 39, showing an immune response to CT, LT and ETA alone in Table 8 (page 39). In view of the experimental results obtained clearly showing an immune response obtained to adjuvant used alone, it is believed the rejection has been overcome and may properly be withdrawn. Acknowledgement of the demonstrated enablement is respectfully requested.

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request reconsideration and the timely allowance of the pending claims. A favorable action is awaited. If, in the opinion of the Examiner, an interview would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the telephone number provided below.

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. § 1.16 and § 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **Constructive Petition for Extension of Time** in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully submitted,
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